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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,165	11/13/2003	Kevin R. Stone	CROL-132CPCN	8206
23630	7590 05/24/2006		EXAM	INER
	OTT WILL & EMERY	AFREMOVA, VERA		
	ATTN: INTELLECTUAL PROPERTY DEPTARTMENT 28 STATE STREET			PAPER NUMBER
BOSTON, MA 02109			1651	

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)
	10/712,165	STONE ET AL.
Office Action Summary	Examiner	Art Unit
	Vera Afremova	1651
The MAILING DATE of this communication ap Period for Reply	pears on the cover sheet with the c	orrespondence address
A SHORTENED STATUTORY PERIOD FOR REPL WHICHEVER IS LONGER, FROM THE MAILING D - Extensions of time may be available under the provisions of 37 CFR 1.1 after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period - Failure to reply within the set or extended period for reply will, by statute Any reply received by the Office later than three months after the mailine earned patent term adjustment. See 37 CFR 1.704(b).	OATE OF THIS COMMUNICATION 136(a). In no event, however, may a reply be tin will apply and will expire SIX (6) MONTHS from e, cause the application to become ABANDONE	N. nely filed the mailing date of this communication. D (35 U.S.C. § 133).
Status		
 Responsive to communication(s) filed on 22 / N This action is FINAL. Since this application is in condition for allowated closed in accordance with the practice under the condition. 	s action is non-final. Ince except for formal matters, pro	
Disposition of Claims		•
4) Claim(s) 1-48 is/are pending in the application 4a) Of the above claim(s) 23-48 is/are withdray 5) Claim(s) is/are allowed. 6) Claim(s) 1-22 is/are rejected. 7) Claim(s) is/are objected to. 8) Claim(s) are subject to restriction and/o	wn from consideration.	
9) The specification is objected to by the Examine 10) The drawing(s) filed on is/are: a) accomposed and applicant may not request that any objection to the Replacement drawing sheet(s) including the correct to be the second and the correct to be the second and the second area of the second and the second area of the second and the second area of the second area.	cepted or b) objected to by the lead of a drawing(s) be held in abeyance. Section is required if the drawing(s) is objection	e 37 CFR 1.85(a). jected to. See 37 CFR 1.121(d).
Priority under 35 U.S.C. § 119		
12) Acknowledgment is made of a claim for foreign a) All b) Some * c) None of: 1. Certified copies of the priority document 2. Certified copies of the priority document 3. Copies of the certified copies of the priority document application from the International Burea * See the attached detailed Office action for a list	ts have been received. ts have been received in Applicationity documents have been received tu (PCT Rule 17.2(a)).	on No ed in this National Stage
Attachment(s) 1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other:	

DETAILED ACTION

Election/Restrictions

Applicant's election of the Group I (claims 1-22) in the reply filed on 3/22/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 23-48 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 1-22 are under examination in the instant office action.

Claim Rejections - 35 USC § 112

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is indefinite with regard to concentration of sialic acid as presently claimed which is indicated as being ".01 mM". It is unclear what amount is intended. Is it 0.1 or 0.001 or else?

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-46 of US 6,972,041 in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise "bone" of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules as required by claimed methods.

Some of the claims of US 6,972,041 are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules, for example: claims 31-33. Some of the claims of the presently claimed invention are drawn to the use of particular capping molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US 6,972,041 and the presently claimed invention are obvious variants. Moreover, the instant invention is not intended to limit capping molecules to

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the exclusive use of sialic acid molecules (see specification page 13, line 7) and it encompasses the use of generic capping molecules including fucosyl and glucosamine in xenografts intended for human transplantation, for example: see claim 2 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

2. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of US 6,455,309 in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise "bone" of "bone blocks" (see US 6,455,309 claims 22, 23 and 25, for example) or "bone" (instant application) of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules as claimed.

Some of the claims of US 6,455,309 are broader and encompass xenografts such as ligament and/or articular cartilage that comprise bones or portion of bones or bone tissue (see claims 21-25, for example) as required for the presently claimed invention. The method of making xenograft products of US 6,455,309 comprises steps of treating xenograft materials with glycosidase and capping with molecules as required by the presently claimed method.

Some of the claims of US 6,455,309 are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules, fro example: claims18 and 19. Some of the claims of the presently claimed invention are drawn to the use of particular capping

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molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US 6,455,309 and the presently claimed invention are obvious variants. Moreover, the instant invention is not intended to limit capping molecules to the exclusive use of sialic acid molecules (see specification page 13, line 7) and it encompasses the use of generic capping molecules including fucosyl and glucosamine in xenografts intended for human transplantation, for example: see claim 2 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

3. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of US 6,402,783 in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise block of "bone" (US 6,402,783) or "bone" (instant application) of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules as claimed.

Some of the claims of US 6,402,783 are broader and encompass xenografts such as ligaments that comprise bones or some portion of bones or block of bones (see claims 9-10, for example) as required for the presently claimed invention. The method of making xenograft

products of US 6,402,783 comprises steps of treating xenograft materials with glycosidase and capping with molecules as required by the presently claimed method.

Some of the claims of US 6,402,783 are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules, for example: claims 2 and 3. Some of the claims of the presently claimed invention are drawn to the use of particular capping molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US 6,402,783 and the presently claimed invention are obvious variants. Moreover, the instant invention is not intended to limit capping molecules to the exclusive use of sialic acid molecules (see specification page 13, line 7) and it encompasses the use of generic capping molecules including fucosyl and glucosamine in xenografts intended for human transplantation, for example: see instant claim 2 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

4. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19, 21-15 and 58 of US 6,231,608 in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended

for human transplantation wherein the xenograft materials comprise "bone tissue" (US 6,231,608) or "bone" (instant application) of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules as claimed.

Some of the claims of US 6,231,608 are broader and encompass xenografts such as ligament and/or articular cartilage that comprise bones or portion of bones or bone tissue (see claims 21-25, for example) as required for the presently claimed invention. The method of making xenograft products of US 6,231,608 comprises steps of treating xenograft materials with glycosidase and capping with molecules as required by the presently claimed method.

Some of the claims of US 6,231,608 are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules. Some of the claims of the presently claimed invention are drawn to the use of particular capping molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US 6,231,608 and the presently claimed invention are obvious variants.

Moreover, the instant invention is not intended to limit capping molecules to the exclusive use of sialic acid molecules (see specification page 13, line 7) and it encompasses the use of generic capping molecules including fucosyl and glucosamine in xenografts intended for human transplantation, for example: see claim 2 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

5. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 US 6,210, 440.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise "bone" (instant application) or block of "bone" of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules such as sialic acid as required by the claimed methods.

The claims of US 6,210, 440 are broader and encompass xenograft products such as ligaments which comprise bones or portion of bones (see claims 6, 7, 15, 16, for example). The whole xenograft products are treated with glycosidase and sialic acid molecules as claimed in the method of issued claims of US 6,210, 440 (B) and as required by presently claimed method of the instant application.

The claims of US 6,2 10, 440 are broader and include the presently claimed concentration ranges of sialic acid, for example: see claim 1 of US 6,210,440 and see instant claim 3. Some of the claims of the instant application appear to be drawn to the use of concentration ranges of sialic acid which are identical to the sialic acid concentration in US 6,210, 440; for example: see claim 1 of US 6,2 10,440 and the instant claim 14.

Accordingly, the claimed methods and products are obvious variants. Thus, the inventions as claimed are co-extensive.

6. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of US 6,110,206.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise "bone" (instant application) or block of "bone" of non-human animal and wherein the xenograft materials are treated with glycosidase as required by the claimed methods.

The claims of US 6,110,206 are broader and encompass xenograft products such as ligaments which comprise bones or portion of bones (see claims 6 and 7, for example). The whole xenograft products are treated with glycosidase as claimed in the method of issued claims of US 6,110,206 and as required by presently claimed method of the instant application.

The claims of 6,110,206 are broader, they are not limited to the use of capping molecules and they are open to incorporation of additional steps or materials. On the other hand, some of the instant claims do not require the use of capping molecules, for example: see claim 1. In addition, the use of some generic capping molecules are intended for making the xenografts of US 6,110,206, for example: see col. 8, lines 13-16.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

7. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of US 6,049,025.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise "bone" (instant application)

or portion of "bone" of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules including sialic acid as required by the claimed methods.

The claims of US 6,049,025 are broader and they encompass making xenografts such as ligaments that comprise bones or portion of bones (see claims 8 and 16, for example). The whole xenograft materials are treated with glycosidase in the method of issued claims and as required by presently claimed method of the instant application.

Some claims of US 6,049,025 are drawn to the use of concentration ranges of sialic acid which are identical to the presently claimed invention, for example: see claims 2 and 11 of US 6,049,025 and see the instant claim 14. Or the claims of US 6,049,025 are broader and include the presently claimed concentration range, for example: see the instant claim 3.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

8. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of US 5,944,755 in view of Merck Index.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended for human transplantation wherein the xenograft materials comprise block of "bone" (US 5,944,755) or "bone" (instant application) of non-human animal and wherein the xenograft materials are treated with glycosidase and capping molecules as claimed.

Some of the claims of US 5,944,755 are broader and encompass xenografts such as cartilage that comprise bones or portion of bones (see claim 8, for example) as required for the

presently claimed invention. The method of making xenograft products of US 5,944,755 comprises steps of treating xenograft materials with glycosidase and capping with molecules as required by the presently claimed method.

Some of the claims of US 5,944,755 are drawn to the use of particular capping molecules such as fucosyl and glucosamine molecules, for example: claims 2 and 3. Some of the claims of the presently claimed invention are drawn to the use of particular capping molecules such as sialic acid molecules. However, the capping molecules such fucosyl, glucosamine and sialic acid are well known compounds widely distributed in animal mucoproteins and mucopolysaccharides as adequately demonstrated by The Merck Index (page 758 and page 1458). Thus, the claimed invention of US 5,944,755 and the presently claimed invention are obvious variants. Moreover, the instant invention is not intended to limit capping molecules to the exclusive use of sialic acid molecules (see specification page 13, line 7) and it encompasses the use of generic capping molecules including fucosyl and glucosamine in xenografts intended for human transplantation, for example: see instant claim 2 and see specification at page 11, lines 26-27.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

9. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of US 5,782,915.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass substantially similar methods of making xenografts intended

for human transplantation wherein the xenograft materials comprise "bone" (instant application) or portion of "bone" of non-human animal and wherein the xenograft materials are treated with glycosidase.

Claims of 5,782,915 are broader and they encompass methods of making xenografts from articular cartilage comprising bones or portion of bones which are required for the presently claimed invention, for example: see claim 2. The issued claims of US 5,782,915 and the presently claimed invention are both drawn to methods of making xenografts that comprise bones or bone portions and that are treated with glycosidase in the methods of making xenografts.

The issued claims of 5,782,915 are broader, they are not limited to the use of capping molecules and they are open to incorporation of additional steps or materials. On the other hand, some of the instant claims do not require the use of capping molecules, for example: see claim 1. In addition, the use of some generic capping molecules are intended for making the xenografts of US 5,782,915, for example: see col. 5, line 28.

Accordingly, the claimed methods are obvious variants. Thus, the inventions as claimed are co-extensive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,231,608 (Stone), US 6,110,206 (Stone), US 6,049,025 (Stone et al), US 5,944,755 (Stone), US 5,782,915 (Stone) and US 5,922,027 (Stone) taken with Merck Index.

Claims are directed to methods of making xenografts intended for human transplantation wherein the xenografts comprise "bone" and/or portion of "bone tissue" of non-human animal and wherein the xenografts are treated with glycosidase and capping molecules. Some claims are/are further drawn to the use of capping molecules such as sialic acid molecules. Some claims are further drawn to the use of particular concentrations of sialic acid in the method of making xenografts. Some claims are further drawn to the use of glycosidase such as galactosidase, to the use of particular concentration of glycosidase, to the freeze/thaw cycles or gamma irradiation for cellular disruption, to the use of cross linking agents in the methods for making xenografts.

The cited patents are relied upon as explained above and they teach the similar concepts of making xenografts intended for human transplantation wherein the xenografts comprise "bone" and/or portion of bone tissue of non-human animal and wherein the xenografts are treated with glycosidase and capping molecules.

For example: US 6,1 10,206 discloses method of making ligament xenograft with the bone attached (see col. 5, lines 11-17) which is treated with glycosidase or alpha-galactosidase and with capping molecules (see examples 1 and 2).

US 5,944,755 discloses method of making articular cartilage xenograft comprising subchondral bone (see col. 5, lines 60-63) which is treated with glycosidase or alphagalactosidase and with capping molecules (see examples 1 and 2).

US 5,782,915 teaches method of making articular cartilage xenograft comprising

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subchondral bone (see col. 4, lines 2 1-22) which is treated with glycosidase (col. 6, line 34) and with capping molecules (col. 5, line 28).

US 5,922,027 teaches method of making an articular cartilage xenograft comprising subchondral bone (see col. 4, lines 23-26) which is free from moieties susceptible to glycosidase digestion (col. 7, line 12) and which is treated with capping molecules (col. 5, line 32).

The cited patents further teach the use of freeze/thaw cycles or gamma irradiation for cellular disruption, the use of cross-linking agents in the methods for making xenografts. For example: See US 6,110,206 at col. 5, 1ines-36, 46 and 62; or See US 5,944,755 at col. 6, lines 17, 28 and 44; or See US 5,782,915 at col. 4, lines 57 and 67; or See US 5,922,027 at col. 4, line 53 and col. 5, line 2.

The cited patents teach the use of various capping molecules in the method of making xenografts including capping molecules such as glucosamines, for example: see US 6,110,206 at col. 8, lines 15-16; or see US 5,944,755 at col. 9, lines 9-11. But the cited patents are silent with regard to the use of sialic acid.

However, the Merck Index teaches that the capping molecules such as glucosamine and sialic acid are well known compounds which are widely distributed in animal mucoproteins and mucopolysaccharides, for example: page 758 and 1458.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use various capping molecules in the method of making xenografts with a reasonable expectation of success in making xenografts suitable for transplantation because various capping molecules including glucosamine and sialic acid are

widely distributed in mucoproteins and mucopolysaccharides of animal tissues and, thus, they considered to be biochemically functional equivalents.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

The cited patents have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, they constitute prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP 706.02(l) (1) and 706.02(l)(2).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

May 22, 2006

VERA AFREMOVA

V. Sfremora

PRIMARY EXAMINER